Doc Code: AP.PRE.REQ

OIPE IAP5 NOV 05 2007 PATENT & TRADEMARK OFFICE

PTO/SB/33 (07-05)
Approved for use through xx/xx/200x. OMB 0651-00xx
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional): 03-278US1

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Mail Stop AF, Commissioner For Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)]

On 11/01/2007

Signature 

Typed or printed name Beth Shadmi

Application Number	Filed
10/664,601	09/18/2003

First Named Inventor: Weenna Bucay-Couto

Art Unit	Examiner
1614	Timothy E. Betton

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest.
See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed.
(Form PTO/SB/96)

☒ attorney or agent of record.
Registration number 42,059.

☐ attorney or agent acting under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

_____
Signature

Keum J. Park
Typed or printed name

908-518-7700
Telephone number

_____
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required.
Submit multiple forms if more than one signature is required, see below*.

☒ *Total of 1 forms are submitted.

This collection of information is required by 35 U.S.C. 132. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11, 1.14 and 41.6. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

OIPE IAP5 NOV 05 2007 PATENT & TRADEMARK OFFICE

Reasons for requesting pre-appellate review:

The Claim Rejection Under 35 U.S.C. 112, first paragraph is Erroneous

Claims 1-4 and 6-21, and 33-37 are rejected under 35 U.S.C. 112, first paragraph as failing to comply with the enablement requirement. This rejection is erroneous. Applicants state that the proper test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPW 214, 219 (CCPA 1976). Applicants state that one reasonably skilled in the art could make or use the invention from the disclosures in the application coupled with information known in the art without due experimentation. Thus, while the Examiner asserts that "[t]he quantity of experimentation needed is substantial...[and] there presents a multiplicity of factors in regard to disclosed agents used in said formulation," Applicants point out that the fact that even if, as the Examiner asserts, experimentation in the area of dosing of chemoablative agents may be complex, this does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd. sub nom., Massachusetts Institute of Technology v. A.B. Fortia,* 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985).

The pending claims were rejected because the Examiner stated that the alleged relevant art (tissue chemoablation) was so unpredictable and that the specification was so devoid of guidance as to how to achieve the claimed tissue necrosis without undue experimentation. Specifically, the Examiner states that

> [t]here is no generalized scheme by which to perform that, which is disclosed in subject claim 1, i.e., ablation and necrosis of said tissue.... There is the presence of working examples insofar as compounding examples, disclosing specific dosage strengths, quantities, and all other related measurements in association with pharmaceutical formulations...The embodiment discloses the processes by which various dosage forms are compounded and manufactured...there is absence as to ***how these formulations ablate and/or necrotize tissue*** (emphasis added).

Thus, it appears that although the Examiner acknowledges that the disclosure teaches ***how to make*** the pharmaceutical formulations of the present invention through the presence of working examples, the specification fails to show ***how the formulations work*** to ablate and/or necrotize tissue.

However, "it is ***not*** a requirement of patentability that an inventor correctly set forth, or even know, ***how or why the invention works***." *Newman v. Quigg*, 877 F.2d 1575, 1581, 11 USPQ2d 1340, 1345 (Fed. Cir. 1989)(emphasis added); *see also Fromson v. Advance Offset Plate, Inc.*, 720 F.2d 1565, 1570, 219 USPQ 1137, 1140 (Fed. Cir. 1983)("[I]t is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests.")

Furthermore, statements that a physiological phenomenon (i.e., "necrosis (death) or shrinkage of nearby tissue upon injection or insertion of the formulation into the tissue;" paragraph [0015]) was observed are ***not inherently suspect*** simply because the underlying basis for the observation cannot be predicted or explained. Therefore, the Examiner erred in suggesting that Applicants are required to explain why the claimed dosage forms cause tissue necrosis of nearby tissue in order to overcome the enablement rejection. Placing such burden on the Applicants to prove how or why their invention works is beyond the purview of the enablement requirement.

As described in the specification, Applicants have made the discovery that the injectable or insertable dosage forms of the present invention that comprises a "chemical ablation agent," when administered in effective amounts, "results in necrosis (death) or shrinkage of nearby tissue upon injection or insertion of the formulation into the tissue." (paragraph [0015]). The dosage forms of the present invention result in "improved dosage retention in the tissue (e.g., there is little to no back-leakage into the injection tract), thereby improving delivery efficiency of the ablation agents and/or minimizing the adverse effects such as nonspecific tissue damage." (paragraph [0014]). Whereas previous "[c]hemo-ablative approaches...lead[s] to nonspecific ablation of both the prostate as well as surrounding tissues and organs," (paragraph [0004]), the dosage forms of the present invention result in cells subjected to the dosage form to die. For example, paragraphs [0016] to [0019] detail the death of cells, for example, by chemo-ablation agents through osmotic stress, free radical attack, or enzyme digestion.

Given that the Examiner rejected the claims as not enabled despite the above disclosure which provides enabling support, it appears that the Examiner questions that the invention has a credible utility. However, the Examiner has the initial burden of challenging a ***presumptively correct assertion of utility*** in the disclosure. Otherwise, the Examiner cannot reject the teachings in the disclosure unless the Examiner has reason to doubt the objective truth of the statements contained in the written description. *In re Brana*, 51 F.3d 1560, 1564 n.12, 34 USPQ2d 1436, 1439 n.12 (Fed. Cir. 1995), *cited with approval in, In re Cortwright,* 165 F.3d 1353, 49 USPQ2d 1464 (Fed. Cir. 1999). Applicants respectfully state that the Examiner has not met this burden.

Finally, the Examiner argues that the "administration of chemical agents on tissue component/cell tissue present[]...complexities in the dynamics of administration" and "unpredictability in the art is significant because of dosage administration issues that persist in the art."

In response, Applicants state that the fact that the field of chemoablation is still being perfected does not preclude one of ordinary skill in the art from making and using the present invention as claimed. Indeed, the Federal Circuit has stated that to comply with 35 U.S.C. 112, first paragraph, it is not necessary to "enable one of ordinary skill in the art to make and use a perfected, commercially viable embodiment absent a claim limitation to that effect." *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1338, 68 USPQ2d 1940, 1944 (Fed. Cir. 2003) (an invention directed to a general system to improve the cleaning process for semiconductor wafers was enabled by a disclosure showing improvements in the overall system). The fact that the Examiner feels that the invention does not work as well as he thinks it should (i.e., he does not feel that the invention is perfected so as to necrotize nearby tissue while minimizing nonspecific tissue damage is not a legal standard.

Indeed, the Federal Circuit has held that "[e]ven if some of the claimed combinations were inoperative, the claims are not necessarily invalid." *Atlas Powder Co. v. E.I. Du Pont De Nemours & Co.,* 750 F.2d 1569, 1576, 224 USPQ 409, 414 (Fed. Cir. 1984). However, in the present case, there is simply no evidence that any of the potential complicating factors that the Examiner proposes, such as "[c]ompromised conditions of tissue" would render the claim inoperable or fail to achieve a particular result. The Examiner has not shown otherwise.

For at least the above reasons, it is respectfully submitted that the specification teaches how to make and to use the invention of the claims and Applicants request withdrawal of the rejection under 35 U.S.C. 112, first paragraph.

The Claim Rejection Under 35 U.S.C. 103(a) based on Hauschild et al. and Escandon et al. in view of Unger I and Unger II is erroneous

Rejection Under 35 U.S.C. § 103(a)

Claims 2-4, 7-21 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,905,475 (Hauschild) and U.S. Patent No. 7,015,253 (Escandon), in view of U.S. Patent Nos. 5,469,854 (Unger I) and 5,733,572 (Unger II). ***Claims 5 and 6 were not rejected as obvious over the cited prior art.***

In response, Applicants state that this rejection is erroneous and was already rendered moot by a previous amendment to the claims.

Applicants note that pursuant to an identical rejection (of the same claims over the same cited art) in the first Office Action dated December 1, 2006, Applicants had previously amended independent claim 1 (upon which the rejected claims depend) to incorporate the features of dependent claim 5, which was not rejected as obvious over the cited prior art. Claim 5 was then cancelled. By such amendment to incorporate the features of a non-rejected claim, this rejection was rendered moot, and thus it appears that this rejection under 103(a) was repeated in the final Office Action in error. Applicants kindly request correction and withdrawal of the rejection.

In addition to the above, the rejection fails because the Examiner has not met his burden of establishing a *prima facie* case of obviousness based upon the prior art. Among other requirements, to establish a *prima facie* case of obviousness, the prior art reference (or references) must teach or suggest all the claim features. *See, e.g.*, MPEP 706.02(j) and the cases cited therein. Hauschild et al., Escandon et al., Unger I and Unger II do not meet this threshold. In addition, rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. *In re Kahn,* 441 F.3d 977, 988 (Fed. Cir. 2006), *cited with approval in, KSR Int'l v. Teleflex, Inc.*, 127 S. Ct. 1727, 1740-41, 82 USPQ 1385,

1396 (2007). Applicants submit that the Examiner has failed to articulate a rational basis for why a person of skill in the art would combine the references in the manner indicated.